Suicide Deaths of Active-Duty US Military and Omega-3 Fatty-Acid Status: A Case-Control Comparison

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ABSTRACT

Background: The recent escalation of US military suicide deaths to record numbers has been a sentinel for impaired force efficacy and has accelerated the search for reversible risk factors.

Objective: To determine whether deficiencies of neuroactive, highly unsaturated omega-3 essential fatty acids (n-3 HUFAs), in particular docosahexaenoic acid (DHA), are associated with increased risk of suicide death among a large random sample of active-duty US military.

Method: In this retrospective case-control study, serum fatty acids were quantified as a percentage of total fatty acids among US military suicide deaths (n = 800) and controls (n = 800) matched for age, date of collection of sera, sex, rank, and year of incident. Participants were active-duty US military personnel (2002–2008). For cases, age at death ranged from 17–59 years (mean = 27.3 years, SD = 7.3 years). Outcome measures included death by suicide, postdeployment health assessment questionnaire (Department of Defense Form 2796), and *ICD-9* mental health diagnosis data.

Results: Risk of suicide death was 14% higher per SD of lower DHA percentage (OR = 1.14; 95% CI, 1.02–1.27; $P < .03$) in adjusted logistic regressions. Among men, risk of suicide death was 62% greater with low serum DHA status (adjusted OR = 1.62; 95% CI, 1.12–2.34; $P < .01$, comparing DHA below 1.75% [n = 1,389] to DHA of 1.75% and above [n = 141]). Risk of suicide death was 52% greater in those who reported having seen wounded, dead, or killed coalition personnel (OR = 1.52; 95% CI, 1.11–2.09; $P < .01$).

Conclusion: This US military population had a very low and narrow range of n-3 HUFA status. Although these data suggest that low serum DHA may be a risk factor for suicide, well-designed intervention trials are needed to evaluate causality.

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Suicide rates among active-duty US military have increased to record numbers, doubling since the inception of Operation Enduring Freedom (Afghanistan) and Operation Iraqi Freedom and rivaling the battlefield in toll on the US military.[1] Army Vice–Chief of Staff General Peter W. Chiarelli described the record suicide rate as "horrible" and voiced frustration that "the Army has not yet been able to identify any causal links among the suicide cases."[2(pA2)]

Deficiencies of nutrients critical for brain function may be a significant contributing risk factor for psychiatric pathology, especially suicide and stress-related psychiatric symptoms.[3] Highly unsaturated omega-3 essential fatty acids (n-3 HUFAs), in particular docosahexaenoic acid (DHA), are selectively concentrated in neural tissues and are required for optimal neural function.[4] These fatty acids cannot be made de novo but are available only from dietary sources, with seafood being the richest source. Nutritional deficiencies in n-3 HUFAs may increase vulnerability to combat deployment stress, manifesting as psychiatric symptoms including adjustment disorders, major depression, impulsive violence, and suicide.[5] In civilian populations, observational studies indicate that low fish consumption is associated with increased risk of completed suicides[6,7] and greater suicidal ideation.[8] Low DHA status was associated with increased risk of past suicide attempts[9] and future suicide attempts.[10] In comparison to placebo, 2 grams per day of n-3 HUFA reduced suicidal thinking and depressive symptoms and reduced the perception of stress among subjects (n = 49) with deliberate self-harm.[11]

These findings suggest that low DHA levels may be a contributing factor for adverse psychiatric symptoms. In this study, we posited that low DHA status would be associated with increased risk of suicide death among military personnel. Prospectively collected serum and supporting data were available from the Armed Forces Health Surveillance Center (AFHSC) for a large number of active-duty suicide deaths (n = 800) and matched controls (n = 800). To our knowledge, this is the largest study of biological factors among suicide deaths.

METHOD

Study Design

This case-control study compared total serum fatty-acid compositions from among 800 randomly selected active-duty US military suicide deaths to 800 matched controls (2002–2008). The AFHSC is a repository of more than 40 million serum samples with matched health data from US military personnel. Data from service members' postdeployment health assessment (Department of Defense [DD] Form 2796, obtained within 6 months of completion of last deployment) closest to the date of serum sample provided information regarding time and theater of deployment (if applicable), exposure to stresses during deployment, self-report of mental health status, and indication for referral to mental health services; demographic data and frozen serum samples were provided by the AFHSC. Mental health and substance abuse–related *ICD-9-CM* diagnosis data reports were similarly obtained.

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Clinical Points

- The status of omega-3 fatty acids is extremely low among US military personnel.
- Low status of docosahexaenoic acid (DHA), an omega-3 fatty acid obtained from seafood and concentrated in the brain, is associated with increased risk for suicide death.
- Ensuring adequate omega-3 nutritional status is likely to benefit, and unlikely to harm, people at risk for suicide.

Selection of Cases and Controls

Suicide deaths were identified among active-duty service members from the Army, Navy, Air Force, and Marines from 2002 through 2008 for whom data and sera were previously collected and available from the Defense Medical Surveillance System and the AFHSC. Cases (n = 800) were included only if confirmed by the Armed Forces Institute of Pathology and officially declared a suicide in the Department of Defense Medical Mortality Registry after detailed investigative review. The index sample date was defined as the date of the serum sample closest to the date of death. All cases selected had a serum sample collected within 12 months prior to suicide. Controls (n = 800) were randomly selected by the AFHSC and matched by age, sex, rank, and availability of a DD Form 2796. Control subjects were selected on the basis of availability of sera drawn within 12 months of the time sera was drawn from their matched case.

Ethics Approval

The institutional review board of the Uniformed Services University of the Health Sciences (Federalwide Assurance [FWA] 00001628; Department of Defense Assurance P60001) granted approval May 8, 2009 (human subjects research protocol HU873B-01).

Sample Analysis

Sera were obtained from the Department of Defense Serum Repository, which receives and stores (at −80°F) residual serum specimens from Department of Defense human immunodeficiency virus testing and programs related to operational deployments worldwide. Serum samples (1,600 samples) were received July 21, 2009, and assayed for total fatty-acid composition utilizing a high-throughput robotic direct methylation coupled with fast gas-liquid chromatography developed and validated by the Section of Nutritional Neurosciences, Laboratory of Membrane Biochemistry and Biophysics, National Institute on Alcoholism and Alcohol Abuse, National Institutes of Health, with interassay variance of < 0.5%.[12,13] Laboratory personnel and principal investigators were masked to case status until all fatty-acid analyses were completed. Fasting status was determined; thus, all fatty acids were expressed as percent of total fatty acids. Fatty-acid degradation in serum samples may have occurred between time of blood draw and freezing. Thus, stability testing was performed by replicating blood draws, serum separation, and quantification of degradation of fatty acids at room temperature for 16 time points over 72 hours. The coefficient of variance for DHA was small (2.1%) and showed no evidence of degradation over 72 hours. Fatty-acid degradation was expected to occur during prolonged freezer storage. Because cases and controls were matched by time of event, the length of storage time for sera was the same, and the proportional degradation of fatty acids was similar.

ICD-9 discharge diagnosis data codes were provided from AFHSC, from all available standardized inpatient data reports or ambulatory data reports. A mental health visit counted as any health care visit that included an *ICD-9* mental health code (*ICD-9* codes 290–219), regardless of the primary visit diagnosis. Visits including substance abuse codes (*ICD-9* codes 292–292 and 303–305) were similarly counted as substance abuse visits. Postdeployment health assessment data from DD Form 2796 were provided by AFHSC and included mental health screening and stress exposure self-report data from previously deployed subjects. However, only 62% of cases had a completed DD Form 2796; in comparison, these data were available for all controls as their selection criteria included having a completed DD Form 2796.

Statistical Methods

We described sample characteristics by age, sex, rank, ethnicity, branch of service, and year of sample. Associations between categorical variables were tested using χ^2 tests. There were differences in ethnicity and branch of service when comparing suicide cases and controls (Table 1), so we adjusted for these factors in subsequent analyses. We assessed the association of items on DD Form 2796 to suicide risk in unadjusted and adjusted logistic regression models. Fatty-acid data were assessed for normality of distribution and population skewing; no outliers were excluded. Fatty-acid data were converted to *Z* scores and entered as continuous variables into logistic regression analyses models. Each individual fatty acid was assessed (eg, increase in *Z* score) for suicide risk. Significance for DHA was not corrected for multiple testing because DHA was identified a priori as our primary hypothesis. The DHA levels were examined first as quartiles, quintiles, octiles, and deciles and then as progressive cutoff levels in adjusted logistic regressions. Analyses were conducted using SPSS software, release 16.0 (SPSS Inc, Chicago, Illinois).

RESULTS

Demographic characteristics are shown in Table 1. For cases, age at death ranged from 17–59 years (mean = 27.3 years, SD = 7.3 years). Differences were present when comparing cases and controls for ethnicity ($P < .001$) and branch of military service ($P < .04$); thus, these factors were included in subsequent analyses. Almost all controls (99.1%) had been deployed, versus 495 of 800 cases (61.9%) who had ever been deployed; therefore, the relationships of deployment number

Table 1. Demographic Characteristics of Study Sample (N = 1,600)

Characteristic	Suicide Deaths (n = 800)	Controls (n = 800)	*P* Value[a]
Age, mean (range), y	27.3 (17–59)	27.3 (18–58)	< 1.0
Active duty, n (%)	800 (100)	800 (100)	< 1.0
Sex, n (%)			< 1.0
Male	765 (95.6)	765 (95.6)	
Female	35 (4.4)	35 (4.4)	
Ethnicity, n (%)			**< .001**
Asian	35 (4.4)	33 (4.1)	
African American	94 (11.8)	127 (15.9)	
Hispanic	66 (8.3)	104 (13.0)	
Native American	22 (2.8)	10 (1.3)	
White	558 (69.8)	503 (62.9)	
Unknown/other	25 (3.1)	23 (2.9)	
Rank, n (%)			< .87
Enlisted	729 (91.1)	729 (91.1)	
Commissioned officer	62 (7.8)	64 (8.0)	
Warrant officer	9 (1.1)	7 (0.9)	
Branch of service, n (%)			**< .04**
Army	361 (45.1)	381 (47.6)	
Air Force	155 (19.4)	147 (18.4)	
Marines	126 (15.8)	153 (19.1)	
Navy	158 (19.8)	119 (14.9)	
Year of suicide death or matched case, n (%)			< 1.0
2002	78 (9.8)	78 (9.8)	
2003	85 (10.6)	85 (10.6)	
2004	103 (12.9)	103 (12.9)	
2005	102 (12.8)	102 (12.8)	
2006	128 (16.0)	128 (16.0)	
2007	144 (18.0)	144 (18.0)	
2008	160 (20.0)	160 (20.0)	
Deployment, n (%)			**< .001**
Never deployed	305 (38.1)	7 (0.9)	
Deployed since 1990	495 (61.9)	793 (99.1)	

[a] χ^2 comparisons. Bold typeface indicates significance.

Table 2. Serum Fatty-Acid Status and Adjusted Odds Ratios of Suicide Death (N = 1,600)[a]

Fatty Acid		Suicide Deaths (n = 800), Mean (SD)	Matched Controls (n = 800), Mean (SD)	Odds Ratio (95% CI)[b]	*P* Value
Omega-3 polyunsaturated fatty acids					
ALA	18:3n-3	0.54 (0.23)	0.55 (0.25)	1.05 (0.95–1.18)	< .30
EPA	20:5n-3	0.44 (0.16)	0.45 (0.17)	1.10 (0.99–1.23)	< .08
	22:5n-3	0.48 (0.13)	0.48 (0.13)	1.03 (0.93–1.15)	< .51
DHA	**22:6n-3**	**1.14 (0.45)**	**1.19 (0.47)**	**1.14 (1.02–1.27)**	**< .03**
Omega-6 polyunsaturated fatty acids					
LA	18:2n-6	31.19 (4.04)	31.39 (4.01)	1.04 (0.94–1.15)	< .43
	18:3n-6	0.40 (0.17)	0.41 (0.16)	1.08 (0.97–1.20)	< .15
	20:2n-6	0.25 (0.05)	0.26 (0.05)	1.10 (0.99–1.22)	< .08
	20:3n-6	**1.61 (0.38)**	**1.68 (0.37)**	**1.18 (1.06–1.32)**	**< .001**
AA	20:4n-6	7.18 (1.87)	7.29 (1.96)	1.03 (0.93–1.15)	< .61
	22:4n-6	0.32 (0.08)	0.32 (0.08)	1.01 (0.91–1.12)	< .85
	22:5n-6	0.23 (0.06)	0.24 (0.07)	1.03 (0.93–1.15)	< .56
Monounsaturated fatty acids					
	16:1n-7	**1.60 (0.68)**	**1.51 (0.61)**	**0.89 (0.81–0.99)**	**< .04**
	18:1n-9	22.95 (3.64)	22.55 (3.71)	0.93 (0.84–1.03)	< .17
	18:1n-7	**2.48 (0.52)**	**2.41 (0.56)**	**0.88 (0.80–0.98)**	**< .03**
	20:1n-9	0.17 (0.05)	0.17 (0.05)	0.95 (0.88–1.05)	< .36
	24:1n-9	1.16 (0.35)	1.15 (0.34)	0.97 (0.88–1.09)	< .62
Saturated fatty acids					
	14:0	0.38 (0.26)	0.41 (0.29)	1.08 (0.97–1.19)	< .19
	16:0	18.44 (2.76)	18.29 (2.91)	0.94 (0.85–1.04)	< .24
	18:0	**6.82 (0.96)**	**7.01 (0.93)**	**1.18 (1.05–1.30)**	**< .003**
	20:0	0.33 (0.06)	0.33 (0.06)	1.04 (0.94–1.15)	< .44
	22:0	1.03 (0.26)	1.05 (0.27)	1.08 (0.97–1.19)	< .18
	24:0	0.85 (0.21)	0.87 (0.22)	1.06 (0.96–1.18)	< .23

[a] Cases and controls were matched for sex, age, rank, and date of blood draw. Fatty acids are expressed as percentage of total serum fatty acids. Bold typeface indicates significant items.
[b] Odds ratios of suicide death per 1 standard deviation for each fatty acid, adjusted for race/ethnicity and branch of service, using multivariate logistic regression.
Abbreviations: AA = arachidonic acid, ALA = α-linolenic acid, DHA = docosahexaenoic acid, EPA = eicosapentaenoic acid, LA = linoleic acid.

and deployment duration with suicide risk could not be appropriately assessed and were not added as covariates.

Our primary hypothesis was that lower n-3 HUFAs, in particular DHA, would be associated with greater risk of suicide. In fact, each standard deviation of lower DHA was associated with a 14% greater risk of suicide (OR = 1.14; 95% CI, 1.02–1.27; $P < .03$, adjusted for race/ethnicity and service component) (Table 2). We sought to determine whether the relationship to suicide risk was uniform across the sample or driven by subgroups with either very high or very low DHA levels. When examining the subjects by octiles, we found that the top octile (n = 200) had a wider range in DHA (1.67%–4.50%) compared to subjects in the middle 6 octiles (n = 1,200) (0.73%–1.66%) or the lowest octile (n = 200) (0.29%–0.73%). Women had a higher DHA percentage compared to men (mean = 1.48%, SD = 0.56% vs mean = 1.15%, SD = 0.45%, respectively; $P < .0001$). However, few women were included in the total sample (n = 70, 4.4%); thus, subsequent analyses were also conducted separately by sex. There were no differences in fatty acids when comparing female cases and female controls.

Only subjects with the highest levels of DHA appeared to be protected; when comparison was made to the highest octile, risk of suicide death was 62% greater among men with lower serum DHA status (adjusted OR = 1.62; 95% CI, 1.12–2.34; $P < .01$, comparing DHA below 1.75% [n = 1,389] to DHA of 1.75% and above [n = 141]). In comparisons to odds in the top octile (n = 179), the odds of suicide death among men were greater in the octile with the lowest DHA percentage (n = 195) (OR = 1.75; 95% CI, 1.14–2.68; $P < .02$), the second octile (OR = 1.52; 95% CI, 1.00–2.32; $P < .054$), the third octile (OR = 1.67; 95% CI, 1.09–2.54; $P < .02$), the fourth octile (OR = 1.57; 95% CI, 1.03–2.39; $P < .04$), the fifth octile (OR = 1.57; 95% CI, 1.02–2.39; $P < .04$), and the sixth octile (OR = 1.77; 95% CI, 1.16–2.70; $P < .02$), but not the seventh octile (OR = 1.48; 95% CI, 0.97–2.26; $P < .07$) (Figure 1).

Lower levels of 2 other fatty acids were associated with increased risk of suicide: 18:0% (stearic acid) and 20:3n-6% (dihomo-γ-linoleic acid [DGLA]) (see Table 2). Higher levels of 16:1n-7% (palmitoleic acid) and 18:1n-7% (*cis*-vaccenic acid) were associated with lower risks of suicide. Lower levels of both eicosapentaenoic acid (EPA) (20:5n-3%) and arachidonic acid (20:4n-6%) were not significantly associated with suicide risk.

Secondarily, we sought to determine whether subjective reports of mental health status were associated with

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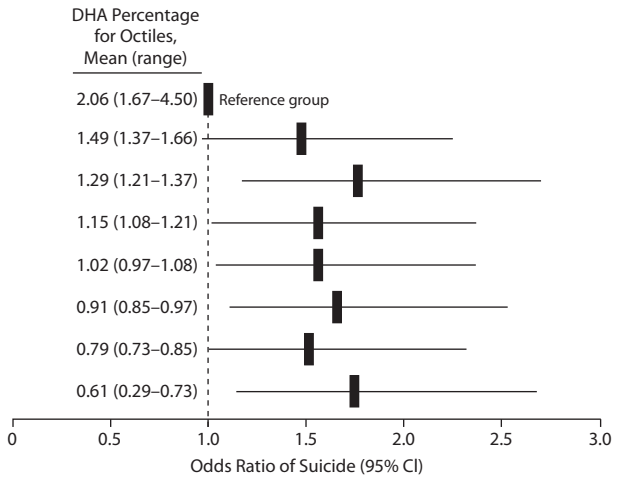
Figure 1. Odds Ratios of Male Suicide Death by Octiles of DHA Status[a,b]



[a]A statistically significant protective effect was observed only in the highest octile compared to each of the lowest 6 octiles.
[b]Odds ratios (95% CIs) are shown in order from highest octile to lowest octile of DHA percentage: Highest octile (reference), seventh octile (OR = 1.48; 95% CI, 0.97–2.26), sixth octile (OR = 1.77; 95% CI, 1.16–2.70), fifth octile (OR = 1.57; 95% CI, 1.02–2.39), fourth octile (OR = 1.57; 95% CI, 1.03–2.39), third octile (OR = 1.67; 95% CI, 1.09–2.54), second octile (OR = 1.52; 95% CI, 1.00–2.32), first (lowest) octile (OR = 1.75; 95% CI, 1.14–2.68).
Abbreviation: DHA = docosahexaenoic acid.

Table 3. Adjusted Odds Ratios of Suicide Death by Postdeployment Questionnaire Items[a]

Item	Adjusted Odds Ratio[b] (95% CI)	*P* Value
Are you interested in mental help?	1.47 (0.80–2.67)	<.21
Do you feel detached?	**1.81 (0.99–3.30)**	**<.05**
Do you have intrusive nightmares?	1.43 (0.89–2.29)	<.14
Do you avoid situations?	**1.76 (1.03–3.00)**	**<.04**
Are you on guard?	1.06 (0.68–1.66)	<.80
Do you avoid conflicts?	1.41 (0.71–2.78)	<.33
Do you lose control?	0.81 (0.32–2.06)	<.66
Did you see any civilians killed?	**1.41 (1.00–1.98)**	**<.05**
Did you see any enemy killed?	1.22 (0.89–1.69)	<.23
Did you see any coalition killed?	**1.52 (1.11–2.09)**	**<.01**
Did you discharge your weapon?	**1.46 (1.03–2.06)**	**<.04**
Did you feel in danger of being killed?	0.96 (0.71–1.29)	<.78
Items answered as "A lot"		
Are you feeling down?	2.10 (0.94–4.70)	<.26
Do you have little interest?	1.35 (0.75–2.43)	<.60
Do you want to hurt yourself?	0.99 (0.00–0.00)	<.99
Items answered as "Some"		
Are you feeling down?	1.67 (0.69–4.69)	<.08
Do you have little interest?	1.19 (0.62–2.28)	<.31
Do you want to hurt yourself?	0.99 (0.00–0.00)	<.99

[a]Postdeployment questionnaire DD Form 2796 data were compared between deployed cases (n = 495) and controls (n = 793). Bold typeface indicates significant items.
[b]Odds ratios, using logistic regression, for risk of suicide death in comparison to a negative response, adjusted for race/ethnicity, age, sex, grade, and branch of service.

increased risk for suicide among deployed subjects. Data from DD Form 2796 were available for almost all controls (99.1%) who had been deployed, versus 495 of 800 cases (61.9%) who had ever been deployed. Cases were more likely to respond "Yes" to the questions "Have you ever had any experience that was so frightening/horrible/upsetting that in the last month you…tried hard not to think about it or went out of your way to avoid situations that reinded you of it?" and "Did you see coalition wounded, killed, or dead during this deployment?" Cases were less likely to respond "Yes" to the question "Were you engaged in direct combat where you discharged your weapon?" (Table 3). No other psychometric responses (eg, thoughts of being better off dead) were associated with increased risk of suicide. Among all subjects, 1 greater SD in the number of mental health visits (mean = 4.8 visits, SD = 12.7 visits) was associated with greater odds of suicide (OR = 1.17; 95% CI, 1.04–1.31; $P < .009$). More inpatient mental health visits (mean = 0.15 visit, SD = 0.53 visit) were more strongly associated with greater odds of suicide death (OR = 1.47; 95% CI, 1.28–1.70; $P < .0001$, per increased SD). History of any visit with substance abuse diagnosis was not associated with suicide (OR = 1.21; 95% CI, 0.90–1.64; $P < .89$). Lower DHA status was not related to number of mental health visits or substance abuse diagnoses.

DISCUSSION

In this study, we found that low DHA status is a significant risk factor for suicide death among active-duty US military. Nearly all US military personnel had low n-3 HUFA status in comparison to North American,[14] Australian,[15] Mediterranean,[16] and Asian[9] populations. The low amounts and narrow range of DHA in this US military population in comparison to world and US diversity made detection of an association difficult and impaired the evaluation of risk relationships among people with higher n-3 HUFA status. For example, the lowest DHA status in a population of suicide attempters in China appeared to be higher than that in nearly all the US military personnel reported here.[9] Chinese subjects in the lowest quartile of DHA status in erythrocytes (mean = 2.72%, range = 0.56%–3.72%) had higher odds of a suicide attempt (OR = 4.76; 95% CI, 1.67–14.28; $P < .0003$) compared to the highest quartile (mean = 6.9%, range = 6.15%–8.94%).[9] When compared across these 2 populations, the lowest DHA status may be associated with a 5- to 6-fold increased risk of suicidal behaviors compared to the highest status. The maximal benefit may not have been assessed in this sample of US military personnel.

Increased risk for suicide is highly likely due to multiple social, psychiatric, and environmental risk factors underscoring the complexity of psychological health issues among service members. The relative impact of low DHA status on increased suicide risk (62%) can be put into perspective in comparison to the relative impact of severe combat stress or prior mental health problems on increased suicide risk. Personnel with a positive report of seeing wounded, killed, or dead coalition personnel during deployment had an increased risk of suicide death of 52% (OR = 1.52; 95% CI, 1.11–2.09; $P < .01$). The strength of the relationship between more numerous prior mental health visits and increased risk of suicide death was also similar to that of low DHA status.

Limitations inherent in this retrospective analysis included the inability to characterize neuropsychiatric symptoms, stress exposure, traumatic brain injury, alcohol use, or other potential risk factors and the inability to assess reverse causality. We noted that an effect of storage time was found for DHA percentage (mean [SD] of 1.32% [0.53%] in 2008 and 1.03% [0.40%] in 2002; $P < .0001$); however, the time of storage was matched for cases and controls. Although unlikely, it is possible that DHA was selectively degraded among cases as compared to controls. Although we would have preferred to use multiple serum samples over time, these were not uniformly available, and the use of a single baseline serum sample robustly protected HUFA status over 12 months' duration when comparing serial samples in a prior study.[17]

As this is a case-control study, we must consider the possibility that the presence of a mental illness or substance misuse has changed dietary habits or tissue status and lowered DHA status. However, in this study we found no differences in fatty-acid status when comparing personnel with and without mental health and substance abuse diagnoses; thus, these diagnoses were unlikely to suggest reverse causality for suicides.

We caution that causality for higher n-3 HUFA status in preventing or treating suicide cannot be inferred from this study alone; however, this interpretation is supported by a randomized placebo-controlled trial[11] of 2 grams per day of EPA and DHA that found a 45% reduction in suicidal thinking and a 30% reduction in depression among patients with recurrent self-harm. Large treatment effect sizes for n-3 HUFAs among subjects with severe depressive symptoms have been reported in several meta-analyses[18–20] of randomized placebo-controlled trials. Severe depressive symptoms are a risk factor for suicidal thinking.[21] Epidemiologic data also indicate that low fish consumption is associated with increased risk for suicide. In a 17-year follow-up study[6] of 256,118 Japanese people, subjects who ate fish less often than every day had a higher risk of suicide compared to subjects who ate fish daily. Among 1,767 Finnish subjects, consuming fish less than twice per week was associated with a higher risk of depressive symptoms and suicidal thinking.[8] Low DHA status also predicted a 3.4-fold greater risk of a new suicide attempt over more than 800 days.[10] These future suicide attempters had greater activity in the anterior cingulate and limbic forebrain in resting positron emission tomography (PET) scans quantifying regional glucose uptake,[22] consistent with the suspected pathophysiology of severe depression and posttraumatic stress disorder. Across a 10-fold range of DHA status (0.7%–7.1% DHA in phospholipids), lower DHA status robustly predicted this regional hyperactivity, indicating that low DHA status may potentially be associated with greater limbic system activity.[22] Mann[23] has linked suicidal and aggressive behaviors and impulsivity to reduced prefrontal cortical activity on PET scans. Supplementation with DHA increases prefrontal activity during sustained attention in a dose-responsive manner.[24]

While this current study could not assess neurobiological mechanisms, several mechanisms are plausible. Serotonergic, dopaminergic, and noradrenergic deficits and overactive stress responses of the hypothalamic-pituitary-adrenal axis are implicated in the neurobiology of suicidal behavior.[23] In piglets, dietary deficiencies of DHA and arachidonic acid for 18 days decreased serotonin, dopamine, and their metabolite levels in the frontal cortex by 50%.[25] In mice, chronic stress induced a 40%–65% decrease in serotonin and norepinephrine levels in the frontal cortex.[26] These results were completely reversed by EPA and DHA supplementation.[25,26] Deficits in synaptoneogenesis and neural plasticity caused by DHA deficiencies may underlie these observations.[27] Observational studies in humans[28,29] are consistent with these animal studies: lower plasma DHA levels correlated with lower cerebrospinal-fluid (CSF) levels of the serotonin metabolite 5-hydroxyindolacetic acid among healthy controls[28] and lower levels of CSF corticotropin-releasing factor in perpetrators of domestic violence.[29]

Unexpectedly, we found that higher DGLA (20:3n-6) status was associated with lower risk of suicide death. In contrast, Virkkunen et al[30] reported that higher phospholipid DGLA levels were associated with a greater likelihood of suicide attempts and violent homicide,[30] and higher DGLA in adipose tissue has been associated with greater depressive symptoms.[31] In this study, we found that lower levels of stearic acid (18:0) were associated with greater risk of suicide and that higher levels of palmitoleic acid (16:1n-7) and *cis*-vaccenic acid (18:1n-7) were associated with lower risk of suicide. The implications of these findings are not clear as psychotropic effects of saturated and monounsaturated fatty acids have not been reported to our knowledge.

Rapidly rising suicide rates are a sentinel for increased impairment of fighting force efficacy due to mental illness.[32] The greatest cause of inpatient bed utilization in the US military is mood disorders, primarily major depression with suicidal risk and adjustment disorders.[33] In response, the US Army has initiated a $50 million observation study[34] enrolling 120,000 subjects per year for 5 years, with the primary purpose of identifying modifiable risk and protective factors related to mental health and suicide. Our identification of low DHA serum status as a significant risk factor for suicide deaths can complement this effort. Low n-3 HUFA status is very likely due to a combination of several factors including excess omega-6 linoleic-acid consumption and deficits in seafood consumption from the foods consumed at US military dining facilities, available restaurants, and choices made at home.[35]

Low DHA status can be readily reversed using low-cost dietary interventions[15] that are likely to have multiple beneficial health effects.[36] The American Psychiatric Association already recommends consumption of at least 1 gram per day of n-3 HUFAs for all patients with psychiatric disorders.[20] The US Food and Drug Administration has determined that up to 3 grams per day of n-3 HUFAs is generally recognized as safe.[37] Evaluation of the efficacy of these levels of n-3 HUFAs in the primary prevention of suicide attempts, or as treatment following suicidal behaviors, merits consideration within the US military.

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